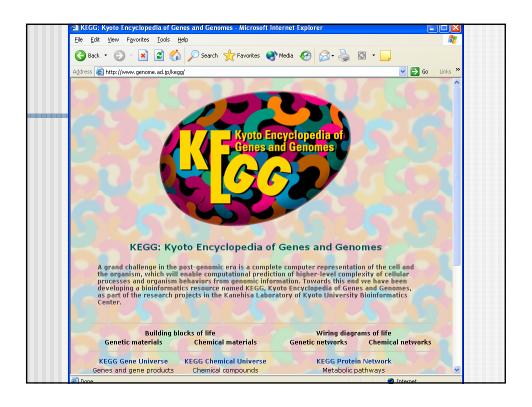
Introduction to Bioinformatics

7. Databases of Genome and pathway networks

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What we will cover today

- Identifying the biological function and context of a gene
- KEGG metabolic database
- Pathway analysis
- Integrate and interpret molecular work within biological context
- http://www.genome.ad.jp/kegg/
- Single nucleotide polymorphism (SNP) identification



KEGG: Kyoto Encyclopedia of Genes and Genomes

- Metabolic Database
- Linked to other databases
 - DBGET (database retrieval system)
 - http://www.genome.jp/dbget/
 - GenomeNet
- Flat file data
- GIF images
- Java graphics
- 3D images

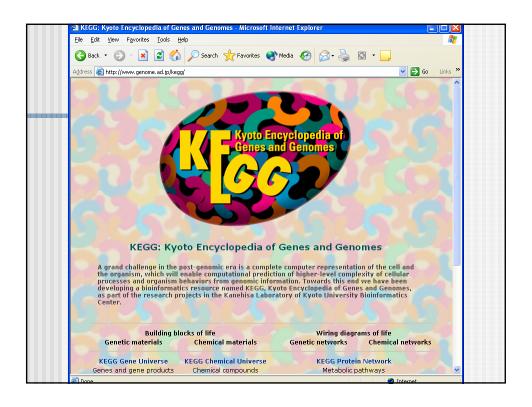
http://www.genome.ad.jp/kegg/

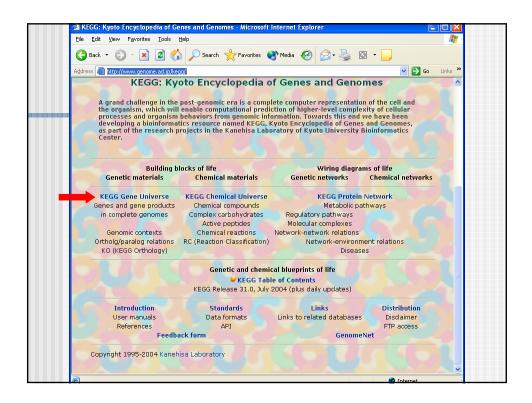
KEGG: Kyoto Encyclopedia of Genes and Genomes

- Linked to sequence interpretation tools
 - BLAST
 - FASTA
 - MOTIF
 - CLUSTALW

What is the function of a gene or gene product?

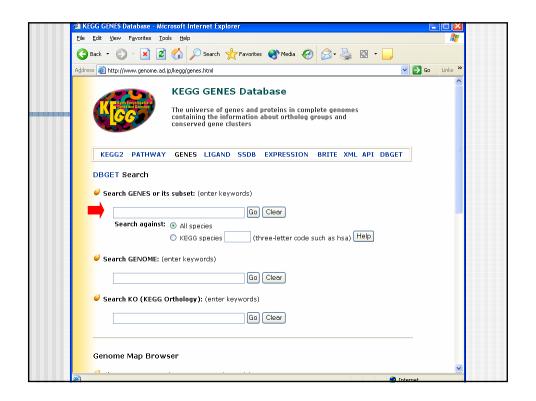
What is its biological Context?

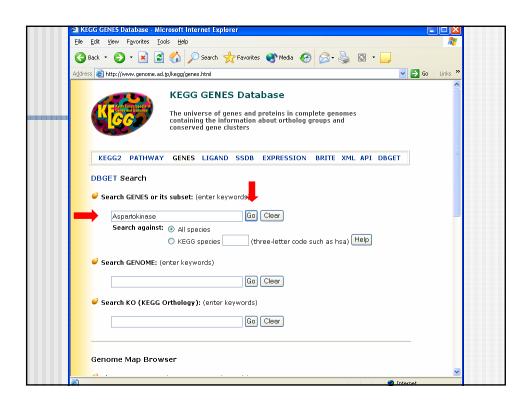


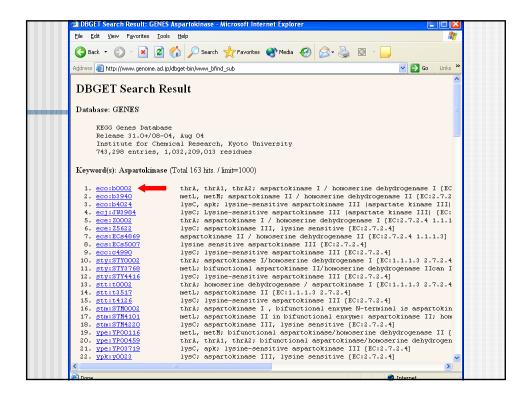


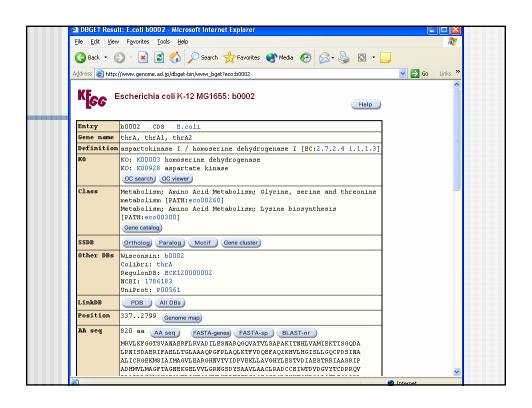
KEGG: Kyoto Encyclopedia of Genes and Genomes

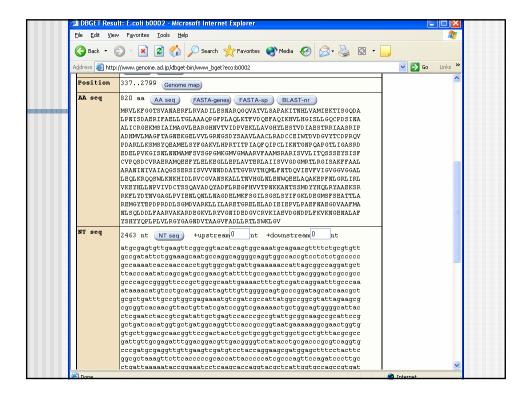
- Gene Universe
 - Genes and gene products
 - Genomic contexts
 - Ortolog/paralog relations
- Chemical Universe
 - Chemical compounds
 - Peptides, carbohydrates
 - Chemical reactions
- Protein network
- Metabolic pathways
- Regulatory pathways
- Networks and complexes

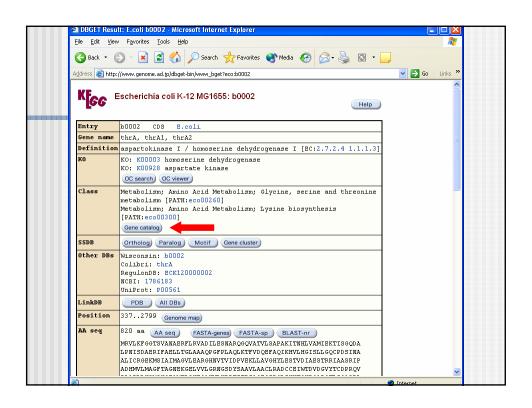


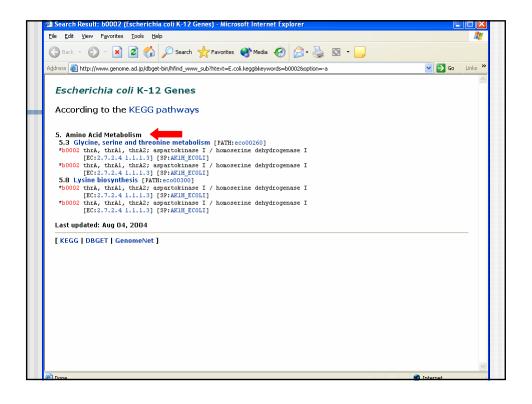


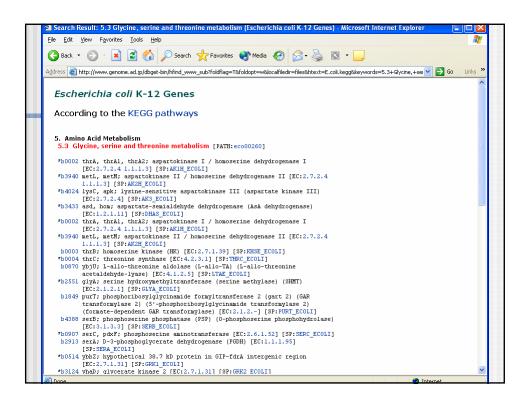


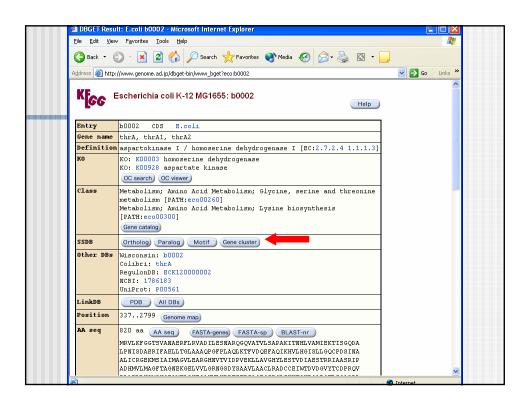


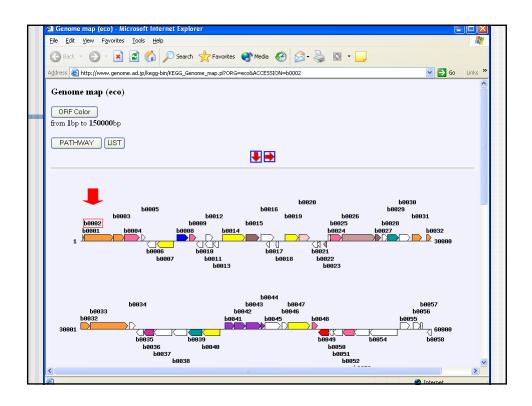


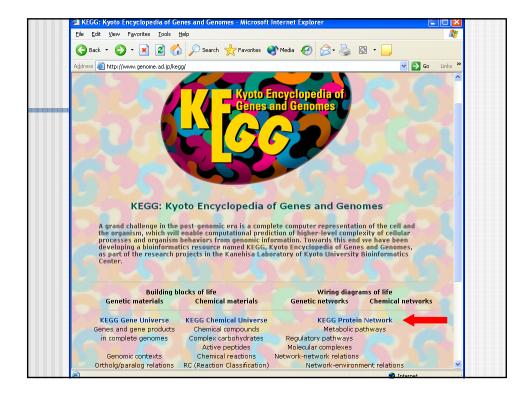


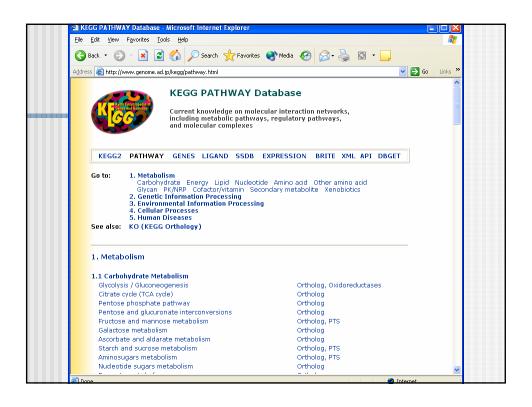


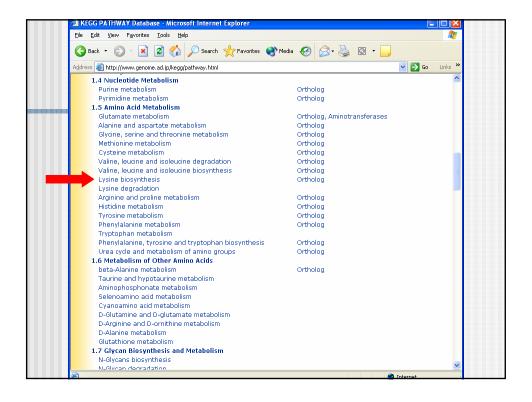


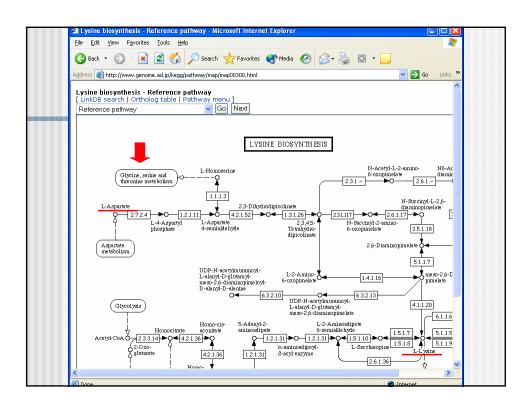


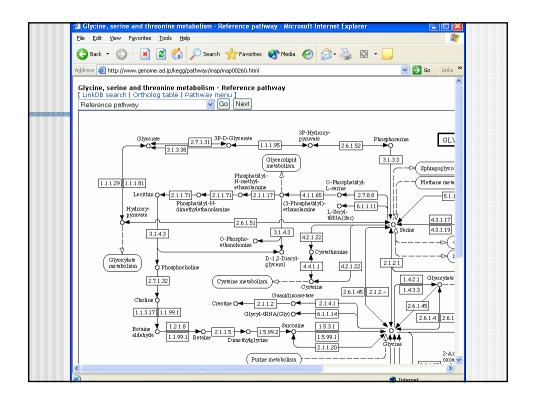


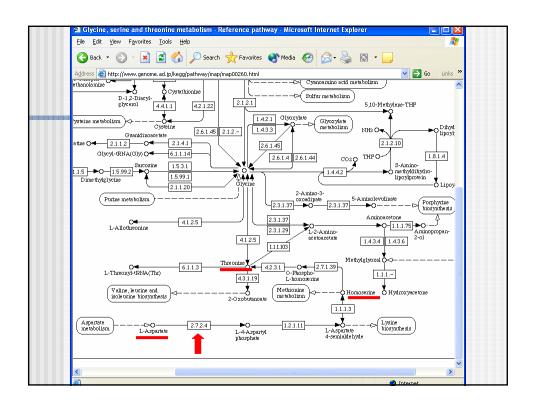


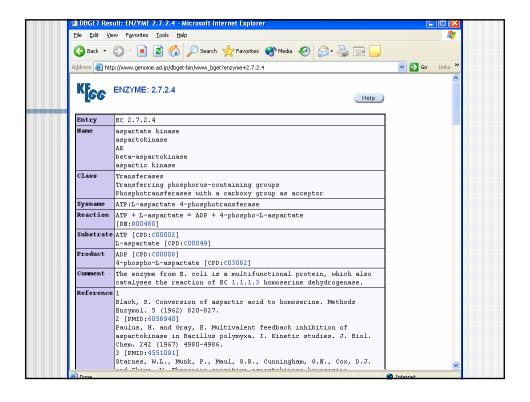


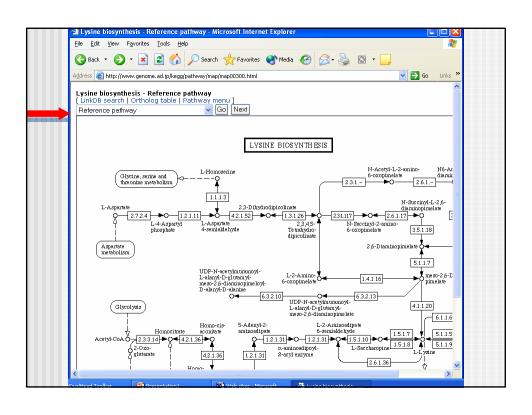


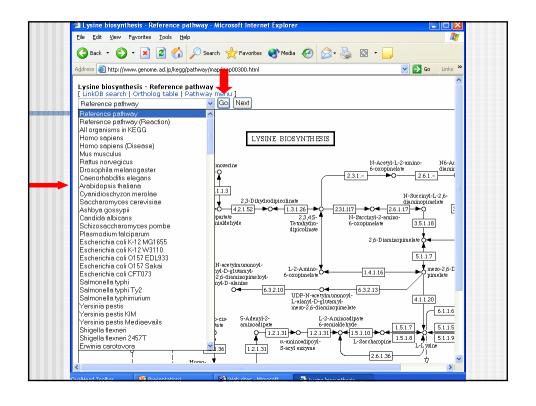


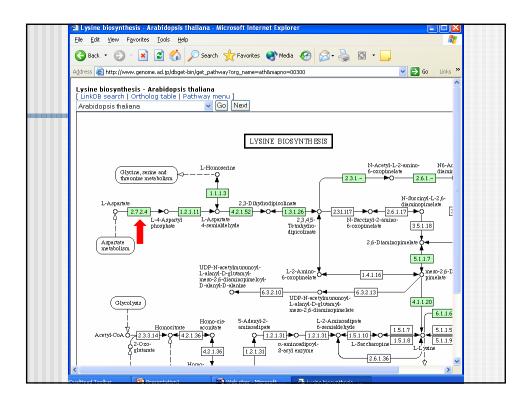






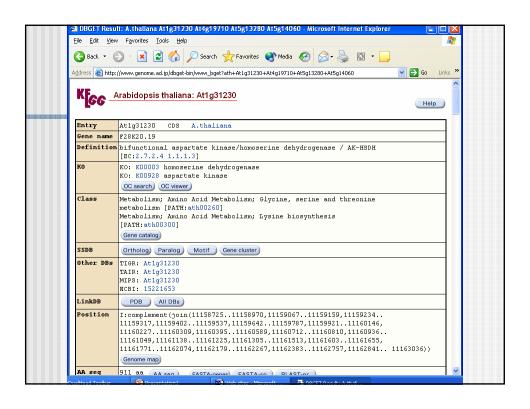


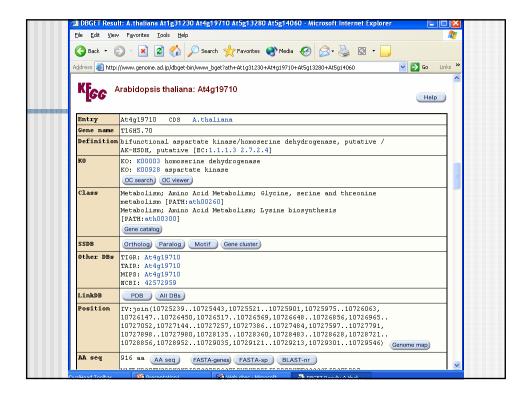




Results

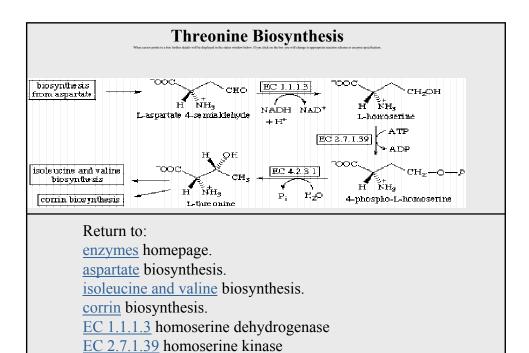
- Four records
 - Two bifunctional aspartate kinase-homoserine dehydrogenases
 - One aspartate kinase
 - One aspartate kinase, lysine sensitive
- Provides amino acid and DNA sequences
- Provides pathway information
- Provides other useful links





Enzyme Nomenclature

- http://www.chem.qmul.ac.uk/iubmb/enzyme/
- Nomenclature Committee of the International Union of Biochemistry and Molecular Biology (NC-IUBMB)
- Reactions and pathways



EC 4.2.3.1 threonine synthase

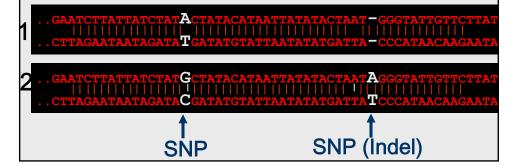
Single Nucleotide Polymorphism (SNP) Discovery

Use of SNPs?

- Genetic mapping
 - Highly abundant markers
 - Easy to assay
- Distinguish plant variety
 - Variety protection
- Phylogenetics

Single Nucleotide Polymorphism

- A working definition -
- Single base changes between homologous DNA fragments
- Small insertions and deletions (indels)

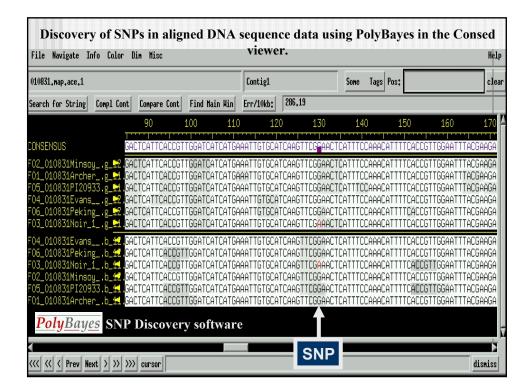


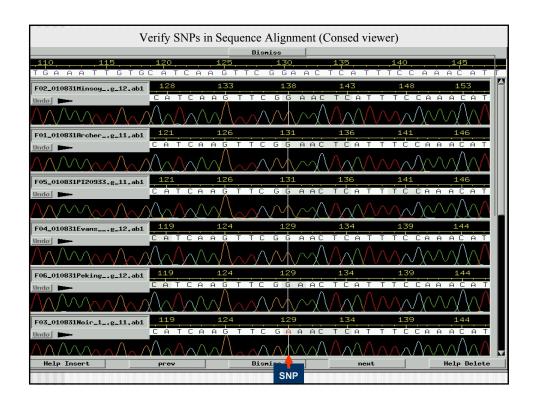
SNPs (Single Nucleotide Polymorphisms)

- Genetic variation
- Can be alleles of genes
- also differences in non-coding regions collected from genome sequencing of different individuals
- dbSNP at the NCBI all public SNP data
- SNP Consortium at CSHL high quality set

SNP Marker Discovery

- 1. Design PCR primers to existing sequence: Complete genes, ESTs, BAC-ends, BAC-subclones, SSR flanking regions, etc.
- 2. Identify sequence tagged sites (STSs) visually (agarose gel) and by sequence analysis
- Amplify the homologous sequence from a panel of diverse genotypes
- Determine sequence quality (PHRED) and align sequence traces (PHRAP) from the diverse genotypes
- Analyze assemblies with SNP discovery software such as PolyBayes for SNP discovery in redundant sequence
- 6. Analyze haplotype variation and database





Data from Consed to SNP Database

- 1. Consensus sequence is created from the Phrap alignment after trimming of bases with Phred score < 25 from each end of sequence.
- 2. The position of each single base change or insertion/deletion (indel) is indicated in the consensus sequence e.g. Single base changes: A/T or G/A and indels: T/- or TCGG/-
- 3. The "haplotypes" that are present in the fragment is determined and the haplotype of each genotype is determined and placed in the database. The haplotype is the linear, ordered arrangement of SNP alleles on a chromosome or DNA fragment.
- 4. Sequence data are placed in the database in a format that allows direct submission to dbSNP, the National Center for Biotechnology Information database for SNP data from all species.

Relational Database Structure

1. Source File:

- a. Information relating to the source of the sequence
- b. BARC sequence ID
- c. PCR primer sequences
- d. optimal PCR conditions
- e. person submitting information

2. SNP File:

- a. Data for each individual SNP
- b. BARC sequence ID
- c. consensus sequence derived from the alignment of alternative

genotypes,

- d. sequence to the 5' side of the SNP
- e. the alternative SNP alleles
- f. the sequence to the 3' side of the SNP

The Source File ence ID 7548 Date entered into database Source ID AB003680 7/31/2002 AB003680 GB Accession # nce Source Genbank Туре gene Association random Comment A3B4 Glycinin Forward Primer AGTGCCCAATATGTTGTCCTCTAC Reverse Primer GTTCGCGTTCAAGTTCCAAT Forward Pr ID 7548 Reverse Pr ID 7546 Conc in mM 3.75 BUFFER: BUFFER: STS-S nnealing Temp 50 Primer Plate Forward primer location ward Pr Conc in uM 0.15 Reverse Pr Conc in uM 0.15 PCR Product Length 551 Seq Data Length ents @ PCR Amplif mments @ sequencing ATAGTAGTGTTTTTGTGGATTTTCAGTGTTAATTAGTGTATCTTCAGAGAA AGAAATAAAAGAAAGCACTAAAACAGGGGGAAAATCATAATTCATAGGTC ATATACCATACAATAAGAAGACATAAAAATGTTAACAAGTATGTTGTAGGG GTTTGTATTCTAAATTTGTGCATTGATTTTTTAAAGTGAGTTTCCACATAT

The SNP File

BARC-GM-00001 Date entered into Database 7/31/2002 Sequence ID 7548 5/31/2002 Date submitted to NCRI SNP Position in consensus Genebank ssal 4473759 SNP postion in consed

> Probability 1 Transtype S

Sequence Source Genbank GB Accession # AB003680 Putative Phenotype Association random Type gene

Comment A3B4 Glycinin

5' side ATTACAAGTAATCAACATGAAACTAATATACGTGCATACTTGCACATCTACCATA AAGAAAGCACTAAAAGAGGGGGAAAATCATAATTCATAGGTCATATACGATACAA TAAGAAGACATAAAAATGTTAACAAGTATGTTGTAGGGTTGGGTTCCTTTTAATG TCATTTAAATTAAATCTCACTTTGATAGATAACTGATTTTTAGAGGTTATGTAGAG GTAATTTTATAGTTATAATGGAGTAAAATTGTTTGTATTCTAAATTTGTGCATTGAT TTTTTAAAGTGAGTTTCGACATATAATT

Submitter name

Youlin

SNP T/C

3' side AAAATATATCATTACCTCTTATTTGATAATAATTAAACATTTATCATTTATATAATAA

Relational Database Structure

- 3. Genotype File:
 - a. BARC sequence ID
 - b. SNP name
 - c. the SNP position in the consensus sequence
 - d. SNP allele present in each genotype
- 4. Haplotype File: (One record for each haplotype for a sequence ID)
 - a. BARC sequence ID
 - b. haplotype ID
 - c. SNP position(s) in the consensus sequence
 - d. the genotype(s) with the haplotype
 - e. the complete sequence of the haplotype

The Haplotype File

14843

Haplotype ID 014843 HAP2

449-476-

Archer_;Minsoy_;

entered into Database

1/3/2003

Submitter Name

Ik-Young

GATACCCTAGATGAAACAGCAAGGAGTGCAGGAAGCACACGCTCCACAAGGTCA CCCAATACAAGAAGGGCAAGGACAGCATCGCCGCTCAGGGAAAACGCCGTTAT GACCGCAAACAGTCCGGTTACGGTGGCCAGACCAAGCCCGTTTTCCACAAAAA GGTACAATTCTACTGTTTCCCCCAAACACTGCCTTATGGTTTTTATTGCTAATAAT TTACTTTTAATTAATTAATTAGGCGAAAACCACCAAGAAAATTGTGTTGAGGCTCCA GTGCCAAGGATGCAAGCATGTCTCGCAGCACGCTATCAAGGTAAAGCATCACTT TCCGTCGTCGTTTTGTATTGTTATTGTGCATGTTTGGTTTACAGTCGAAAATGCTG CTGTGCACGAACCAATGCAAATCCAATGAATAAAAGTAAAATGAACGCAGAAGTGT TGGCAAAATTACTTTTGCCTCAAACAGTAATTTTGCAACTGATTCCCAAACATGCT CATTGCCGTTTTGAACACGTGGTTGATGCTTGCTATGTGGTTCTGTTTTGCAGAG

GATACCCTAGATGAAACAGCAAGGAGTGCAGGAAGCACACGCTCCACAAGGTCA CCCAATACAAGAAGGCAAGGACAGCATCGCCGCTCAGGGAAAACGCCGTTAT GACCGCAAACAGTCCGGTTACGGTGGCCAGACCAAGCCCGTTTTCCACAAAAA GGTACAATTCTACTGTTTCCCCCAAACACTGCCTTATGGTTTTTATTGCTAATAAT TTACTTTTAATTAATTAATTAGGCGAAAACCACCAAGAAAATTGTGTTGAGGCTCCA GTGCCAAGGATGCAAGCATGTCTCGCAGCACGCTATCAAGGTAAAGCATCACTT TCCGTCGTCGTTTTGTATTGTTATTGTGCATGTTTGGTTTACAGTCGAAAATGCTG CTGTGCACGAACCAATGCAAATCCAATGAATAAAAGTAAAATGAACGCAGAAGTGT TGGCAAAATCACTTTTGCCTCAAACAGTAATTTTGCAACTGATTCCCAAACATGCT CATTGCCGTTTTGAACACGTGGTTGATGCTTGCTATGTGGTTCTGTTTTGCAGAG GTGCAAGCACTTTGAGATCGGTGGTGACAAGAAGGGAAAAGGAACATCTCTCTT CTAGATGGAATATTAGAATTTGCAATTTCACACACTCTCTGTACTTTTCTCAGTTT GATTGCCACGGG

The Genotype File

Sequence ID 7548

BARC-GM-00001

SNP Position

SNP position before trimming

Minsoy

Evans T

PI209332 C

Pelaing T

Poly McN 1

Poly MkA 1

Poly 209x Evans 0

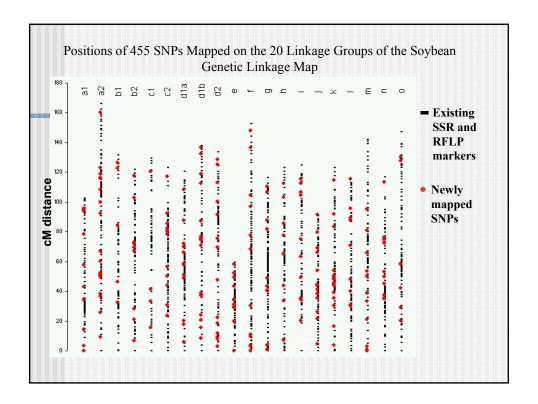
Poly six genotypes ()

Date entered into Database

7/31/2002

Submitter name

Youlin



What we covered today

- KEGG Metabolic database
- Pathway analysis
- Integrate and interpret molecular work within biological context
- http://www.genome.ad.jp/kegg/
- Single nucleotide polymorphism (SNP) identification